

CLAIMS:

1. A pharmaceutical formulation comprising:
(1) a therapeutically effective amount of active nasal peptide,
5 its pharmaceutically acceptable salt or its peptidic fragment;
and (2) the absorbefacient and stabilizer THAM
[tris(hydroxymethyl) aminomethane]; in a pharmaceutically
acceptable, aqueous liquid diluent or carrier, said formulation
being in a form suitable for nasal administration.
- 10 2. The pharmaceutical formulation, according to claim 1,
wherein the nasal peptide, its pharmaceutically acceptable salt
or its peptidic fragment is selected from the group of peptide
hormones or hormone derivatives, physiologically active
15 lymphokines or monokines, peptidic enzymes, proteic vaccines,
peptidic toxoids, personalised proteins derived from genoma,
which can be conveniently used in a form suitable for nasal
administration.
- 20 3. The pharmaceutical formulation, according to claim 1 or 2,
wherein the nasal peptide, its pharmaceutically acceptable salt
or its peptidic fragment is selected from the group of peptide
hormones or hormone derivatives such as buserelin, desmopressin,
vasopressin, angiotensin, felypressin, octreotide, somatropin,
25 thyrotropin (TSH), somatostatin, gosereline, thryptorelin and
insulin (from cow and pig or synthetic or recombinant).
4. The pharmaceutical formulation, according to claim 1 or 2,
wherein the nasal peptide, its pharmaceutically acceptable salt
30 or its peptidic fragment is selected from the group of peptide
hormones or hormone derivatives such as protirelin,
adrenocorticotropin (ACTH), prolactin, luteinizing hormone (LH),
luteinizing hormone-release hormone (LH-RH), leuprorelin,

calcitonin (human, chicken, eel, porcine or recombinant),
carbocalcitonin and calcitonin gene related peptides (CGRP).

5. The pharmaceutical formulation, according to claim 1 or 2,
5 wherein the nasal peptide, its pharmaceutically acceptable salt
or its peptidic fragment is selected from the group of peptide
hormones or hormone derivatives such as kallikrein, parathyrin,
glucagon, oxytocin, gastrin, secretin, leptin, nafarelin, serum
gonadotropin, gonadotropin release factor, growth hormone,
10 erythropoietin, hirudin, urogastrone, renin and human parathyroid
hormone (h-PTH)

6. The pharmaceutical formulation, according to claim 1 or 2,
wherein the nasal peptide, its pharmaceutically acceptable salt
15 or its peptidic fragment is selected from the group of
physiologically active lymphokines or monokines such as
interferon, interleukin, transferrin, histaglobulin,
macro cortine, endorphins, enkephalins and neurotensin.

20 7. The pharmaceutical formulation, according to claim 1 or 2,
wherein the nasal peptide, its pharmaceutically acceptable salt
or its peptidic fragment is selected from the group of peptidic
enzymes such as lysozyme, urokinase and superoxide dismutase.

25 8. The pharmaceutical formulation, according to claim 1 or 2,
wherein the nasal peptide, its pharmaceutically acceptable salt
or its peptidic fragment is selected from the group of proteic
vaccines as acellular and cellular pertussis, diphtheria, tetanus
and influenza vaccines.

30 9. The pharmaceutical formulation, according to claim 1 or 2,
wherein the nasal peptide, its pharmaceutically acceptable salt
or its peptidic fragment is selected from the group of peptidic

toxoids such as diphtheria, tetanus and from the group of personalised proteins derived from genoma.

10. The pharmaceutical formulation, according to any one of the
5 preceding claims, wherein (1) the therapeutically effective amount of active nasal peptide, its pharmaceutically acceptable salt or its peptidic fragment is in concentrations of 0.001 microgram/ml to 50.0 mg/ml or of 10 Units/ml to 20000 Units/ml, in relation to the therapeutically effective dose to be
10 administered by endonasal route; and (2) THAM is in concentrations of 0.5 mg/ml to 30.0 mg/ml.

11. The pharmaceutical formulation, according to any one of the preceding claims, wherein (1) the therapeutically effective
15 amount of active nasal peptide, its pharmaceutically acceptable salt or its peptidic fragment is in concentrations of 0.01 microgram/ml to 50.0 mg/ml or of 20 Units/ml to 12500 Units/ml; and (2) THAM is in concentrations of 2.0 mg/ml to 10.0 mg/ml.

20 12. The pharmaceutical formulation, according to any one of the preceding claims, wherein (1) the therapeutically effective amount of active nasal peptide, its pharmaceutically acceptable salt or its peptidic fragment is in concentrations of 0.05 microgram/ml to 10.0 mg/ml or of 100 Units/ml to 6000 Units/ml;
25 and (2) THAM is in concentrations of 2.5 mg/ml to 4.5 mg/ml.

13. The pharmaceutical formulation, according to any one of the preceding claims, wherein said pharmaceutical formulation is in the form of ready-to-use or of reconstituted solution suitable
30 for nasal administration in the form of a drop type or of a nasal spray.

14. The pharmaceutical formulation, according to any one of the preceding claims, suitably administrable in a metered single dose

volume or in multiple doses thereof, said actuation comprising a metered dose volume between 50 microliters and 200 microliters.

15. A method for producing a pharmaceutical formulation
5 according to any one of the preceding claims, wherein the aqueous liquid diluent or carrier comprises optionally other pharmaceutically acceptable auxiliary additives such as (a) hydrochloric or citric acid; (b) one or a mixture of methyl or/and propyl p-hydroxybenzoate; and (c) cysteine

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16. The method according to claim 15, wherein the pharmaceutically acceptable, aqueous liquid diluent or carrier further comprises optionally other pharmaceutically acceptable auxiliary additives such as (a) hydrochloric acid 0.1 N in
15 concentrations of 0.3 mg/ml to 50.0 mg/ml or citric acid in concentrations of 0.6 mg/ml to 60.0 mg/ml, more preferably of 2.8 mg/ml to 6.2 mg/ml; (b) one or a mixture of methyl or/and propyl p-hydroxybenzoate in concentrations not exceeding 0.3 mg/ml with a ratio of 2:1 to 20:1; and (c) cysteine in concentrations of 0.5
20 mg/ml to 10.0 mg/ml.

17. A method for producing a pharmaceutical formulation for nasal administration according to any one of claims 1 to 14, in the form of ready-to-use solution, said method comprising the
25 steps of: adding an adequate amount of distilled water to THAM, and optionally to methyl or/and propyl p-hydroxybenzoate, hydrochloric or citric acid and cysteine until complete dissolution; then dissolving at the end the adequate quantity of nasal peptide or its pharmaceutically acceptable salt or its
30 peptidic fragment in said solution mixture.

18. The method according to claim 17, which further includes the step of: filtering to make the solution suitable for nasal administration and filling a mono-disposable, or multidose device

system with the filtrate, more preferably with progressive dose counting system.

19. A method for producing a pharmaceutical formulation for nasal administration, according to any one of claims 1 to 14, in the form of reconstituted solution, said method comprising:

preparing container n.° 1 with the nasal peptide either by dosing in the container the corresponding weight of powder of active nasal peptide or by preparing a suitable solution with a known concentration of the same, pouring the individually dosed volume into the container and then lyophilizing it to yield a lyophilized powder;

preparing container n.° 2 comprising the solvent mixture for reconstitution, resulting from adding an adequate amount of distilled water to THAM, and optionally to methyl or/and propyl p-hydroxybenzoate, hydrochloric or citric acid and cysteine until complete dissolution;

filtering to make the solution suitable for nasal administration; and

filling container n.° 2 with the filtrate.

20. The method according to claim 19, wherein container no .° 1 is prepared by dosing directly in the container the corresponding weight of powder 1e), or by preparing a suitable solution with a known concentration of the same, pouring the individually dosed volume directly into the container and then lyophilizing it directly in the container to yield a lyophilized powder.

21. The method according to claim 19 or 20, which further includes the step of: preparing the reconstituted solution at the time of starting its use by pouring the solvent mixture of container n.° 2 into container n.° 1; mixing thoroughly by rotation until complete dissolution; screwing the multidose

device system on the neck of container n.° 1, comprising the reconstituted solution.

22. The pharmaceutical formulation, according to any one of
5 claims 1 to 14, which have long shelf life, and when in-use, provide compositions of a therapeutically effective amount of active nasal peptide, its pharmaceutically acceptable salt or its peptidic fragment.
- 10 23. A method for treating, with a pharmaceutical formulation according to any one of claims 1 to 14, a patient which comprises intranasally administering in the form of drop type or of nasal spray to said patient, a dosed volume of said formulation,
15 comprising a therapeutically effective amount of nasal peptide or of its pharmaceutically acceptable salt or peptidic fragment conveniently combined with THAM in a pharmaceutically acceptable liquid, aqueous carrier or diluent, with the scope to elicit the desired pharmacological effect.
- 20 24. The method, according to claim 23, in which the administrable dose volume of the pharmaceutical formulation, comprised in a metered monodose disposable or in a multidose system thereof, is comprised between 50 microliters and 200
25 microliters per actuation.